
GENERAL REVIEW AND ENFORCEMENT POLICIES

FOOD ADDITIVE PETITION REVIEW

I. Introduction

Section 201(s) of the Federal Food, Drug, and Cosmetic Act (Act) defines the term "food additive" and lists the five specific exceptions from this definition. One of these exceptions is "a new animal drug." Section 409 of the Act contains the provisions governing food additive petitions.

Parts 170 through 189 of the Code of Federal Regulations (21 CFR) implement the Act with respect to food additives for human consumption; Parts 570 through 589 implement the Act for food additives for animal consumption.

Once the original has been filed, subsequent submissions of a Food Additive Petition are considered amendments to the original petition. Regardless of the type, the review procedure, including time frames, shall be the same.

The statutory requirements for review of food additive petitions (FAPs) are different from those for new animal drug applications (NADAs). Therefore, the administrative review process for FAPs is different from that for NADAs.

Section 571.1(i)(1) of the regulations requires that the sponsor of a food additive petition be notified within 15 days after receipt of the acceptance or non-acceptance of the petition for filing. Section 571.1(i)(2) directs that a Notice of Filing be published in the FEDERAL REGISTER within 30 days after the petition is filed.

Section 409(c)(2) of the Act requires that an order establishing a regulation for the food additive or denying the petition be issued within 90 days after the petition is filed. The 90-day period may be extended to 180 days by written notice to the petitioner. If a food additive petition is amended by the petitioner with data determined to constitute a substantive amendment, the amended petition may be given a new filing date, and the time limitations outlined above will begin again.

A. Overview of Critical Time frames for Action on a Food Additive Petition.

<u>Time frame(s)</u>	<u>Description of Action Required</u>
0 days	CVM receipt date
15 days	Issue letter of acceptance or non acceptance (date of issuance = date of filing).
30 days	Publish Notice of Filing in the FEDERAL REGISTER. Mail a copy of the Notice to the petitioner.
90 days	Issue written notice to the petitioner to extend 90-day period to 180 days, or publish order of approval or denial if review is completed.

Note: All time frames are in calendar days.

II. Receipt of Petition and Initial Review

The initial review of the FAP must be accomplished within 15 calendar days of the CVM receipt date. In order to allow the reviewing officer ample time to meet the statutory time limitations, the FAP must be handled rapidly from the moment of receipt.

A. Logging in a FAP

Document Control Unit (DCU), (HFV-199) receives the original submission, assigns it a FAP number, and stamps the date of receipt on it. The DCU Data Transcriber enters the FAP number into STARS. DCU sends the petitioner an acknowledgement letter of receipt and notice of FAP number. DCU also receives any amendments and correspondence related to the FAP, date stamps them, and enters them into STARS.

The original FAP (or other submission) is hand carried to the Director, Division of Animal Feeds. The submission is logged in and forwarded directly to the primary reviewing officer. The processing time from receipt in DCU to the reviewing officer should be not more than one day.

B. Initial Review

The reviewing officer will determine if the petition is acceptable for filing. The Environmental Assessment Team (HFV-145) should be consulted regarding the appropriateness of Section H for public display and comment. The Environmental Assessment Team will provide such a consultation within 5 days. The petitioner is to be notified in writing within 15 days of the CVM receipt date of acceptance or non-acceptance of the petition for filing.

III. Determination of Acceptance or Non-acceptance for Filing

Each FAP is submitted in triplicate and includes the data and information requested under Section 571.1(c) of the regulations. The petition is carefully reviewed to ascertain whether or not the data requested under each subparagraph (A-H) are present.

A. Non-acceptance

If any of the subparagraphs are not addressed or if Section H may be initially determined inadequate for meaningful public review and comment, the petition will not be filed, and a letter of non acceptance will be issued within 15 days of the CVM receipt date.

1. Document Summary

A document summary is prepared to explain the reasons for nonacceptance, e.g., not all data requested under 571.1(c) appear in the petition.

2. Letter of Non-acceptance

The following stock paragraph is an example of appropriate language for the non-acceptance letter which will be signed by the Director, Division of Animal Feeds.

Your Food Additive Petition FAP# dated regarding has been received and has been found nonacceptable for filing. The petition does not contain information as provided for under 21 CFR 571.1(c) (A, B, C, D, E, F, G, or H). (Specify the information needed.) Upon receipt of the appropriate information, we will again review your petition for acceptability for filing. Please refer to the above FAP number in future correspondence.

3. Issuance of Non-acceptance Letter

The non-acceptance letter will issue within 15 days of the date of receipt of the FAP. The letter will be issued by the Division of Animal Feeds, and the petition will be returned to DCU. (The petition will be retained in CVM and is not returned to the petitioner.) The non-acceptance letter will state that certain information contained in the FAP is available for public disclosure under Section 571.1(h), even though the petition has not been filed.

4. Conversion to Investigational File

If the deficiencies in the petition are significant, the non acceptance letter may recommend that the petitioner convert the FAP to an investigational file to complete the work required for acceptance and approval of the petition.

5. Resubmission to an Unfiled Petition

If the petitioner amends the unfired petition to alleviate deficiencies identified in the non-acceptance letter, an additional 15 days is available to determine the acceptability of the petition for filing.

6. Request to File as Submitted

The petitioner may request that the petition be filed as submitted, with no amendment or explanation. In this case, the petition is filed and the petitioner is notified of the filing by letter. The procedures followed are the same as for acceptance for filing (see 3.B. and 4). If no further, information is submitted, and the petition remains deficient, an order of denial will be published (see 10. A.).

B. Acceptance

If the requested data are present, Section H is sufficiently complete for meaningful public review and comment, and cursory review indicates that the petition is acceptable for filing, the reviewing officer shall prepare and issue a letter acknowledging the acceptance of the FAP for filing. This letter must issue within 15 days of the CVM receipt date.

1. Document Summary

A document summary is prepared for the issuance of the acceptance letter. It gives the basis for the determination of acceptance, e.g., that all parts of 21 CFR 571.1(c) have been submitted.

2. Letter of Acceptance

The following stock paragraph is an example of appropriate language for the acceptance letter which is signed by the Director, Division of Animal Feeds, HFV-220.

"Your Food Additive Petition dated _____ regarding _____ has been received and assigned FAP# _____. Please refer to this number in any future correspondence.

The petition has been found acceptable for filing. The date of issuance of this letter is the date of filing for purposes of Section 409(b)(5) of the Federal Food, Drug, and Cosmetic Act. A Notice of Filing will appear in the FEDERAL REGISTER within 30 days. A copy of the notice will be mailed to you.

Further action on the petition awaits scientific review and evaluation. We will notify you within 90 days of its status as required by 21 CFR 571.100.

21 CFR 571.1(h) specifies those data and information in your petition which will become available for public disclosure once the Notice of Filing appears in the FEDERAL REGISTER. Comment from the public will be invited concerning subparagraph H, Environmental Assessment of your petition."

3. Issuance of Acceptance Letter

The acceptance letter will be issued within 15 days of receipt of the FAP in CVM. The letter will be issued by the Division of Animal Feeds. The file will be retained by the reviewing officer.

4. Preparation of Notice of Filing for Publication in the FEDERAL REGISTER, and Requests for Consulting Reviews

Once a determination of acceptance for filing has been made, the reviewing officer will immediately determine the need for consulting reviews, and will initiate preparation of a Notice of Filing for publication in the FEDERAL REGISTER. Under Section 409(b)(5) of the Act, the Notice of the regulation proposed by the petitioner shall be published in general terms by the Secretary within thirty (30) days after filing. The date of the acceptance letter is the date of filing.

A. Preparation of the Notice

Concurrent with the issuance of the letter accepting the petition for filing, the reviewing officer will submit the FAP to the Policy and Regulations Team (HFV-6) for preparation of the Notice of Filing. HFV-6 will draft the Notice of Filing and work directly with the reviewing officer to agree on the text. HFV-6 will return the draft notice to the Division of Animal Feeds for concurrence. The Division of Animal Feeds will forward the draft through HFV-230 to the Regulations Editorial Staff (HF-27) for preparation of the final document.

B. Issuance of the Notice

The FEDERAL REGISTER Notice of Filing will be circulated as follows (hand-carrying is recommended):

HFC-222 (Final Notice)

HFV-6

HFV-228/222

HFV-220

HFV-152

HFV-200

HFV-230

HFV-1 (Signature) (Returns jackets to HFV-228/222)

GCF-1

HF-27 (Regulations Editorial Staff Publication)

While circulating, a copy of the FAP will routinely accompany the Notice of Filing.

GCF-1 will designate a specific attorney as the contact person for this FAP. The reviewing officer will file copies of the FEDERAL REGISTER Notice in the FAP (Original, Duplicate and Triplicate).

C. Consulting Reviews

Requests for consulting reviews will be made within 5 days from the date of issuance of the acceptance letter, if a determination has been made that such reviews are needed. Under Section 409(c)(2), the order establishing or denying a petition will be issued within 90 days after the date of filing of the petition. Since this is an extremely short period of time for in-depth scientific review and administrative processing of a petition, the importance of requesting consulting reviews as early as possible is readily apparent. The need for additional copies of the petition may also be apparent when multiple consulting reviews are needed. The consultant will be apprised of the 90-day requirement. The 90 days can be extended to 180 days, but it requires written notice to the petitioner.

V. Review of the Petition

The types of data required in food additive petitions are set forth in Section 571.1(c) (A-H) of the regulations. While the actual content may vary from petition to petition, each of the following subject areas will be addressed in either the primary or consulting reviews.

A. Chemical Identity

The information on chemical identity will be reviewed by a chemist or other scientist.

B. Amount of Food Additive Proposed for Use and Its Purpose(s)

The information, accompanying data, and labeling submitted under this section will be reviewed by a scientist whose training and experience qualify him/her to assess the intended physical or other technical effect(s) of the food additive.

C. Intended Physical or Other Technical Effect (Utility)

The information and accompanying data submitted under this section will be evaluated by a scientist and a statistician, if necessary, to assure that the data, including controls, are adequate. Generally, one dose titration study and two confirmation studies will be required.

D. Feed Assay

Any information and data on method(s) for feed assay will be evaluated by a chemist.

E. Animal and Human Safety

Qualified scientists will review all human and animal safety data in accordance with Center guidelines.

F. Tolerances

Qualified scientists will review all tissue residue data and any proposed tolerances for the food additive in edible tissues in edible tissues.

G. Proposed Regulation

The reviewing officer will compare the proposed regulation against the supporting data and assure that all species, claims, and physical or technical effects are supported by adequate data.

H. Environmental Assessment (EA)

The Environmental Assessment Team (HFV-145) will review the report. Section 25.31 of the regulations describes the general provisions of environmental impact considerations for food additive petitions. The EA is made available to the public

(at the Dockets Management Branch, HFA-305), at the time the FAP is filed and comments received on the EA must be considered.

VI. Freedom of Information

Under Section 571.1(h), information, other than that considered confidential, contained in a food additive petition is available for public disclosure after the Notice of Filing is published in the FEDERAL REGISTER. If the petition is not promptly filed because of deficiencies, the information is releasable after the petitioner is informed that it will not be filed because of the deficiencies involved.

Rather than routinely purging all food additive petitions for this purpose, the Center for Veterinary Medicine will request that those persons wishing to examine a food additive petition do so by appointment.

As a part of the final regulation approving the food additive, the following paragraph will be included:

"In accordance with Section 571.1(h) (21 CFR 571.1(h)), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Veterinary Medicine (address above) by appointment with the information contact person listed above. As provided in 21 CFR 571.1(h)(2), the Agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection."

The contact person named in the document will coordinate with the Center Freedom of Information Officer in the Office of Management and Communications to determine the information required to be purged from the file prior to disclosure. The contact person will be responsible for arranging a suitable place for the file to be reviewed. DCU will be the repository for purged files in the event of future requests for disclosure.

Unlike NADAs, no FOI Summary is required for FAPs since most of the data in the FAP is releasable. Section 20.60 through 20.64 identify the kinds of information exempt from public disclosure.

VII. Bioresearch Monitoring

The standard operating procedures for processing a food additive petition as regards bioresearch monitoring activities are as follow:

Prior to the full review of the safety and utility data, the reviewing officer will obtain the following information from the petition and forward it to the Bioresearch Monitoring Program Manager (HFV-234) to determine if the particular petition contains data from studies conducted under the bioresearch monitoring program.

- A. The name of the petitioner, the FAP number, and any related INADs (investigational food additives).
- B. A list of any clinical investigators involved.
- C. A list of non-clinical laboratories involved in the petition.

If a check of the records indicates no problems with studies conducted under the bioresearch monitoring program, a statement will be put in the reviewer's first review as follows:

"Bioresearch records in HFV-234 were reviewed and contain no basis for refusal to approve this petition (or amended petition)."

This statement will later be incorporated into the action memorandum.

If a problem is uncovered during a check of the bioresearch monitoring records, the pertinent facts will be discussed with the Director, Division of Animal Feeds for resolution before proceeding with any further review of the data involved.

Under Section 571.1(k), the petition is required to contain a statement regarding compliance with Part 58 (GLPs) of the regulation.

VIII. Written Notice to Extend 90-day Period to 180-Days

In order to facilitate communications between the Center and the petitioner and to satisfy statutory requirements, written notification will be sent to the petitioner whenever the 90-day statutory time limitations will be exceeded. The emphasis will be on providing written information to the petitioner prior to the expiration of the statutory time limit.

A. Extending 90 Days

In situations where the statutory time limit for review of the FAP will exceed 90 days, written notification will be sent to the petitioner prior to 90 days from the date of filing. The following paragraph may be used:

"We have not completed our evaluation of the petition at this time and conclude that we will be unable to complete our study and investigation of the petition within the 90 days specified by Section 409(c)(2) of the Act. We are, therefore, extending this period for an additional 90 days as provided for in 409(c)(2) because (reason)."

B. Document Summary and Issuance of Extension Letter

A brief document summary which explains the reason for the delay should accompany the 90-day extension letter. The letter is to be signed by the Director or Deputy Director, Division of Animal Feeds. Once the letter is issued, the petition is to be retained by the reviewing officer.

IX. Written Notice to Establish a New Filing Date

Section 571.6 provides that if the petitioner amends the FAP with data that the Commissioner determines to be a substantive amendment, the petition as amended will be given a new filing date, and the time limitations will begin to run anew. Since the original filing date was established by written notice (letter), the new filing date must likewise be established by written notice (letter).

Theoretically, the petition can be amended at any time. Depending upon when the amendment is received, the nature of the amendment, the extent to which the review of the unamended petition has progressed, and the impact of the amendment on our ability to meet statutory time limitations, the reviewing officer should recommend whether or not to establish a new filing date. A new filing date should never be established without good reason.

If the Director, Division of Animal Feeds decides to establish a new filing date, a document summary and letter (signed by the Director or Deputy Director, Division of Animal Feeds) will be prepared explaining the basis for the decision. The date of issuance of the letter becomes the new filing date. The letter will be issued within 15 days of receipt of the amendment in CVM. Issuance is the same as issuance of the acceptance letter (see 3.B.).

X. Decision to Approve or Deny the Petition

Based upon a complete review of the petition, a recommendation to approve or deny the proposed regulation will be made by the reviewing officer.

A. Decision to Deny Approval

A document summary will be prepared to explain the basis for conclusions reached regarding parts A-H of 21 CFR 571.1(c). Discretion will be exercised when determining whether to issue an incomplete letter or to publish a denial order in the FEDERAL REGISTER. Technically, we cannot incomplete the petition, but will either publish an order describing the conditions under which the food additive may be safely used or publish an order denying the petition. However, the use of an incomplete letter has gained acceptance within and without the agency, and its use is recommended.

1. Incomplete Letter

If deficiencies in the petition appear to be resolvable, it is preferable to offer the petitioner the opportunity to amend the petition (per 571.7). An incomplete letter (signed by the Director, Division of Animal Feeds) can be used for this purpose. The incomplete letter will be issued by DAF, and the petition will be returned to the DCU. If the petitioner opts to amend the petition, the time limitations will begin anew. The petitioner may also opt to withdraw the petition without prejudice to future filing (21 CFR 571.7).

2. Withdrawal of Petition Without Prejudice

At any time before the order provided for in Section 571.100(a) has been forwarded to the FEDERAL REGISTER for publication, the petitioner may withdraw the petition without prejudice to a future filing according to 21 CFR 571.7(b).

a. Preparation of Notice of Withdrawal

Upon receipt of a letter requesting withdrawal, the reviewing officer will send the FAP to HFV-6 for preparation of a Notice of Withdrawal. HFV-6 will draft the Notice of Withdrawal and work directly with the reviewing officer to agree on the text. HFV-6 will return the draft notice to HFV-228/222 for concurrence. HFV-228/222 will forward the draft through HFV-230 to the RES, HF-27 for preparation of the final document.

b. Issuance of the Notice

No specific time frames are required for issuance of the Notice of Withdrawal; however, it is recommended that the time frames for Notice of Filing be adhered to, that is, within 30 days of the CVM receipt of a letter by the petitioner requesting withdrawal of their FAP. Circulation of the Notice of Withdrawal is similar to the Notice of Filing with the exception that HFV-230 will send the document by courier to GCF-1 for their concurrence. The petition will be returned to HFV-228/222, and the reviewing officer will ask HFV-199 to file copies of the FEDERAL REGISTER Notice in the FAP.

3. Order of Denial

Under Section 409(c)(1)(B) of the Act, the Secretary (Center Director) shall by order deny the petition and shall notify the petitioner (by letter) of such order and the reasons for such action. The denial order will be published in the FEDERAL REGISTER and will be prepared and circulated following the same procedures as are detailed for an approved order (see X. B. 1-5).

Normally, this course of action will be taken as a last resort, or in cases where the petitioner obviously cannot satisfy the requirements for approval. This avenue will also be considered for petitions which have been in an inactive status for extended periods of time (often for many years), and the petitioner does not commit to timely reactivation.

The petitioner (or any other person adversely affected by the denial order) will be given the opportunity to submit objections to the order and to request a public hearing on issue (see XII).

B. Decision to Approve

If the petition has been reviewed and found acceptable for approval, the reviewing officer will request that HFV-6 draft a regulation for use of the food additive. The reviewing officer will prepare a document summary, briefing memorandum, and an approval letter for the Center Director's signature. (Note: For approvals involving novel or controversial issues, the functions of the Commissioner have not been redelegated to the Center Director. See 21 CFR 5.61(b)(2).)

1. Preparation of Draft FEDERAL REGISTER Approval Order

The reviewing officer will send the FAP to HFV-6 for preparation of the draft order (or final rule). HFV-6 will be apprised of the time limitations involved.

2. Preparation of a Document Summary

The document summary, prepared by the primary reviewing officer, will reference any consulting reviews and will highlight the conclusions reached under Parts A-H of 21 CFR 571.1(c).

3. Preparation of an Briefing Memorandum

A briefing memorandum will accompany the approval package. The briefing memo will be addressed to the Center Director (HFV-1) through the Director, Office of Surveillance and Compliance (HFV-200). The briefing memo will be signed by the Director, Division of Animal Feeds.

4. Preparation of an Approval Letter (Optional)

The approval letter is signed by the Center Director. The purpose of the letter is to notify the petitioner of the order prior to the forwarding of the order to the FEDERAL REGISTER for publication under 21 CFR 571.100(a).

5. Issuance of the Approval Package

The draft and final FEDERAL REGISTER orders and approval letter with accompanying briefing memorandum and supporting documentation, including the

FONSI/EA or EIS, are circulated for concurrence and signature as follows:

HFV-6 (Draft Regulation)

HFV-228/222

HFV-220

HFV-230 (Returns jackets to HFV-228/222)

HFV-6

HFV-228/222

HFV-200

HFV-230

HFV-1 (Letter Issues), (Returns jackets to HFV-228/222),
(Final Regulations signed by Center Director)

HF-27 (Regulations Editorial Staff Publication)

HFV-228/222 will file copies of the published regulation in the
FAP (Original, Duplicate and Triplicate).

XI. Regulation Issued on Secretary's (Commissioner's) Initiative

A. Proposal

The Secretary (Commissioner) may at any time, upon his/her own initiative, propose the issuance of a regulation, with respect to any particular use of a food additive, prescribing the conditions under which such additive may be safely used, and the reasons therefore.

B. Regulation

After the 30th day following publication of such proposal, the Secretary may by order establish a regulation based upon the proposal.

XII. Objections and Public Hearing

Any person has 30 days after the publication of an order (whether the order establishes a regulation or denies a petition) to file objections thereto with the Secretary (Commissioner) and to request a public hearing upon such objections. Any order must provide for a 30-day comment period. The letter to the petitioner and the FEDERAL REGISTER order (for approval or denial) shall contain notice of the opportunity for a hearing. The filing of objections and hearing procedures related to food additive regulations are governed by 21 CFR Part 12.